

**IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA**

NATERA, INC.,

Plaintiff,

v.

NEOGENOMICS LABORATORIES, INC.,

Defendant.

C.A. No. 1:23-cv-629

JURY TRIAL DEMANDED

**DEFENDANT NEOGENOMICS LABORATORIES, INC.’S ANSWER TO PLAINTIFF
NATERA, INC.’S FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT**

Defendant NeoGenomics Laboratories, Inc. (hereinafter “NeoGenomics” or Defendant”), answers and responds to each of the allegations in the First Amended Complaint for Patent Infringement (“Amended Complaint”) of Plaintiff Natera, Inc. (“Natera”). Unless expressly admitted, NeoGenomics denies each and every allegation in Natera’s Amended Complaint. To the extent the allegations in the Amended Complaint purport to characterize the nature or contents of the Exhibits to the Amended Complaint, NeoGenomics lacks sufficient knowledge or information to form a belief as to the truth of those allegations and on that basis denies them. Additionally, to the extent that the headings or any other non-numbered statements in the Amended Complaint contain any allegations, NeoGenomics denies each and every such allegation.

OVERVIEW OF THE ACTION¹

1. This action arises under the patent laws of the United States, 35 U.S.C. §§ 1, *et seq.*, from Defendant's infringement of Natera's U.S. Patent Nos. 11,530,454 (the "'454 Patent") and 11,319,596 (the "'596 Patent") (collectively, "Asserted Patents").

Answer to First Amended Complaint No. 1:

NeoGenomics expressly denies that any NeoGenomics product or any of its activities fall within the alleged scope of any claim of U.S. Patent Nos. 11,530,454 (the "'454 Patent") and 11,319, 596 (the "'596 Patent") (collectively, "Asserted Patents") or otherwise constitute infringement. NeoGenomics admits that the Amended Complaint purports to state an action for infringement of the '454 and '596 Patents. Except as expressly admitted herein, NeoGenomics denies each and every allegation in paragraph 1 of the Amended Complaint.

THE PARTIES

2. Plaintiff Natera is a corporation organized and existing under the laws of the state of Delaware.

Answer to First Amended Complaint No. 2:

NeoGenomics admits that Natera is a corporation organized and existing under the laws of the state of Delaware.

3. Founded in 2004, Natera (f.k.a. Gene Security Network) is a pioneering genetics and bioinformatics company with industry-leading healthcare products. Natera is dedicated to improving disease management for oncology, reproductive health, and organ transplantation. For well over a decade, Natera has been researching and developing non-invasive methods for

¹ For the Court's convenience, NeoGenomics generally adopts the headings used in Natera's First Amended Complaint. In so doing, NeoGenomics does not admit that the headings are accurate, and reserves the right to contest any statement or characterization set forth under them. To the extent the headings constitute allegations requiring a response, they are denied.

analyzing DNA in order to help patients and doctors manage diseases. These ongoing efforts have given rise to a number of novel and proprietary genetic testing services to assist with life-saving health management.

Answer to First Amended Complaint No. 3:

Paragraph 3 of the Amended Complaint contains statements of opinions to which no response is required. To the extent paragraph 3 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

4. Natera's pioneering and ongoing innovation is especially evident in the area of cell-free DNA ("cfDNA")-based testing. In the cfDNA field, Natera has developed unique and highly optimized cfDNA-based processes that can be used to test non-invasively for a range of conditions. Natera created an industry-leading cfDNA test, Panorama, which showcases Natera's mastery of cfDNA in the field of non-invasive prenatal testing. Natera has also applied its cfDNA testing platform to the challenge of assessing cancer. Natera has developed its cfDNA technology for approval in the clinical setting in order to provide patients with tools for early, clinically meaningful cancer assessment. Natera was awarded approval for coverage by Medicare for multiple indications.

Answer to First Amended Complaint No. 4:

Paragraph 4 of the Amended Complaint contains statements of opinions to which no response is required. To the extent paragraph 4 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

5. In detecting and monitoring cancer, the use of non-invasive, blood-based tests offers significant advantages over older methods, such as invasive tumor biopsy. But the significant technological challenge is that such blood-based testing requires the measurement of very small amounts of relevant genetic material—circulating-tumor DNA (“ctDNA”)—within a much larger blood sample. Natera’s approach combines proprietary molecular biology and computational techniques to measure genomic variations in tiny amounts of DNA, representing a fundamental advance in molecular biology.

Answer to First Amended Complaint No. 5:

Paragraph 5 of the Amended Complaint contains statements of opinions to which no response is required. To the extent paragraph 5 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

6. Natera’s cfDNA platform is the product of well over a decade of hard work and investment of, on average, more than fifty million dollars per year in research and development. Natera has expended substantial resources researching and developing its technologies and establishing its reputation among physicians, insurers, and regulators as a company committed to sound science and consistently accurate, reliable results. This research, and the technological innovations resulting therefrom, are protected by a substantial patent portfolio, with over 330 patents issued or pending worldwide, including greater than 60 in the field of oncology.

Answer to First Amended Complaint No. 6:

Paragraph 6 of the Amended Complaint contains statements of opinions to which no response is required. To the extent paragraph 6 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations,

and therefore denies each and every allegation in that paragraph.

7. Among these patented inventions include the '454 Patent and the '596 Patent, each of which Defendant infringes. Defendant has used Natera's patented cfDNA technology without permission and in violation of the patent laws.

Answer to First Amended Complaint No. 7:

Denied. NeoGenomics specifically denies that it has committed the alleged acts of infringement or that NeoGenomics "used Natera's patented cfDNA technology." NeoGenomics further denies that the Asserted Patents claim "patented inventions."

8. Defendant NeoGenomics Laboratories, Inc. is a corporation organized and existing under the laws of the State of Florida. Upon information and belief, NeoGenomics Laboratories, Inc. operates laboratories throughout the United States, including in Durham, North Carolina.

Answer to First Amended Complaint No. 8:

NeoGenomics admits that it is a corporation organized and existing under the laws of the State of Florida. NeoGenomics further admits that it operates laboratories throughout the United States, including in Durham, North Carolina.

9. Upon information and belief, Defendant NeoGenomics Laboratories, Inc. is a corporate affiliate of both Inivata, Inc. and Inivata Ltd. (collectively, "Inivata"). Defendant NeoGenomics Laboratories, Inivata Inc., and Inivata Ltd. are each wholly-owned subsidiaries of parent corporation NeoGenomics, Inc.

Answer to First Amended Complaint No. 9:

Defendant NeoGenomics Laboratories, Inc. admits that Inivata, Inc. and Inivata Ltd. are each wholly owned subsidiaries of Defendant NeoGenomics Laboratories, Inc. Defendant NeoGenomics Laboratories, Inc. further admits that it is a wholly owned subsidiary of

NeoGenomics, Inc.

10. Defendant operates under and identifies with the trade name “NeoGenomics” and “NeoGenomics Laboratories.” Upon information and belief, Defendant directly or indirectly makes, uses, offers to sell and/or sells in the United States an assay that infringes at least one valid claim of each of the Asserted Patents, including in the State of North Carolina and in this District, and otherwise purposefully directs activities to the same.

Answer to First Amended Complaint No. 10:

NeoGenomics admits that it operates under and identifies with the trade name “NeoGenomics” and “NeoGenomics Laboratories.” Except as so admitted, NeoGenomics denies the remaining allegations in paragraph 10.

11. Instead of developing its own science for its cancer detection and monitoring products, Defendant has unlawfully used Natera’s patented technology, including in connection with the RaDaR™ Minimum Residual Disease Assay and any other products or assays that use the same or similar technology (collectively, “RaDaR” or “Accused Assay”).

Answer to First Amended Complaint No. 11:

NeoGenomics denies each and every allegation in paragraph 11. NeoGenomics specifically denies that it has used or is using Natera’s patented technology.

JURISDICTION AND VENUE

12. This Court has subject matter jurisdiction over the matters asserted herein under 28 U.S.C. §§ 1331 and 1338(a).

Answer to First Amended Complaint No. 12:

NeoGenomics admits that this Court has subject matter jurisdiction over causes of action for alleged patent infringement pursuant to 28 U.S.C. §§ 1331 and 1338(a).

13. NeoGenomics Laboratories is subject to this Court's personal jurisdiction at least because it directs the operations of a CAP/CLIA-certified laboratory located in Durham, North Carolina. In addition, NeoGenomics Laboratories is subject to this Court's personal jurisdiction because, on information and belief, Defendant, directly or indirectly, designs, develops, makes, uses, offers for sale, and/or sells the Accused Assay throughout the United States and within this District. Defendant has infringed and continues to infringe Natera's patents in this District by, among other things, engaging in infringing conduct within and directed at or from this District and purposely and voluntarily placing its infringing assay into the stream of commerce with the expectation that the infringing assay will be used in this District.

Answer to First Amended Complaint No. 13:

The allegation of personal jurisdiction in paragraph 13 constitutes a legal conclusion that requires no response.

14. Upon information and belief, venue is proper in this District pursuant to 28 U.S.C. §§ 1391 and 1400(b) because, among other things, NeoGenomics Laboratories has a regular and established place of business in this District at its CAP/CLIA-certified laboratory located in Durham, North Carolina and has committed acts of infringement at this same location.

Answer to First Amended Complaint No. 14:

The allegation of proper venue in paragraph 14 constitutes a legal conclusion that requires no response.

BACKGROUND

15. Since 2004, Natera has been a global leader in genetic testing, including cfDNA testing. Natera's mission is to improve the management of disease worldwide, and it focuses on reproductive health, oncology, and organ transplantation. To improve the management of these conditions, Natera has developed novel technologies to make significant and accurate clinical

assessments from the miniscule amounts of cfDNA present in a single blood sample. These technologies include methods to manipulate cfDNA in nonconventional ways in order to capture information about genetic variations in cfDNA and usefully transform that information for noninvasive testing. Natera develops and commercializes innovative, non-traditional methods for manipulating and analyzing cfDNA, and offers a host of proprietary cfDNA genetic testing services to the public to assist patients and doctors in evaluating and tracking critical health concerns.

Answer to First Amended Complaint No. 15:

Paragraph 15 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 15 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

16. Since its founding, Natera has researched, developed, and released ten molecular tests with applications in prenatal, cancer, and organ transplants, many of which are available through major health plans, or covered by Medicare or Medicaid, and therefore available to most patients in need of those tests. Natera's tests have helped more than four million individuals to date. Natera's robust laboratory now processes over 130,000 tests per month in the United States and internationally, improving the ability of physicians to monitor and manage crucial health issues and patients to prosper around the world.

Answer to First Amended Complaint No. 16:

Paragraph 16 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 16 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and

therefore denies each and every allegation in that paragraph.

17. Building on these innovations, in 2017, Natera launched its cfDNA test to detect and monitor cancer, called Signatera®. Signatera is a personalized ctDNA surveillance tool that detects molecular residual disease (“MRD”) when assessing disease recurrence or treatment response in solid tumors. Signatera is designed to screen for multiple tumor-derived targets with each assay. It is optimized to detect extremely low quantities of ctDNA and provides early knowledge of disease recurrence with a >99.5% clinical test specificity.

Answer to First Amended Complaint No. 17:

Paragraph 17 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 17 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

18. MRD assessment has become a standard of care in the management of patients with hematological malignancies, but until recently it has not been possible in solid cancers due to technical limitations. Accurate MRD testing and molecular monitoring offers the potential for physicians to change or escalate treatment in patients who are MRD- positive, and to de-escalate or avoid unnecessary treatment in patients who are MRD- negative. It also holds potential as a surrogate endpoint in clinical trials.

Answer to First Amended Complaint No. 18:

Paragraph 18 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 18 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

19. Natera's technology has been validated in multiple clinical studies. In Cancer Research UK/University College London's Tracking Cancer Evolution through Therapy ("TRACERx"), Natera's technology was used for the multi-year monitoring of patient-specific single-nucleotide variants ("SNVs") in plasma, to understand the evolution of cancer mutations over time, and to monitor patients for disease recurrence. Results from the first 100 early-stage lung cancer patients analyzed as part of the study were featured on the cover of the May 2017 issue of Nature and showed that an early prototype version of Signatera identified 43% more ctDNA-positive early-stage lung cancer cases than a generic lung cancer panel and demonstrated its potential to detect residual disease, measure treatment response, and identify recurrence up to 11 months earlier than the standard of care, with a sensitivity of 93% at time of relapse.

Answer to First Amended Complaint No. 19:

NeoGenomics admits upon information and belief that Natera's technology was used in Cancer Research UK/University College London's Tracking Cancer Evolution through Therapy ("TRACERx") study led by Charles Swanton and Miriam Jamal-Hanjani among others. Paragraph 19 of the Complaint otherwise contains statements of opinions to which no response is required. Except as so admitted, to the extent paragraph 19 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

20. The U.S. Food and Drug Administration ("FDA") recognized the importance of Natera's Signatera and has granted it three "Breakthrough Device" designations ("BDDs") for multiple cancer types. The first BDD was awarded on May 6, 2019 to help accelerate FDA assessment and review of Signatera as an *in vitro* companion diagnostic to a certain cancer therapy. In 2021, the FDA granted two additional BDDs covering new intended uses of the Signatera test

to support its development through Phase III clinical trials as a companion diagnostic to different cancer therapies.

Answer to First Amended Complaint No. 20:

Paragraph 20 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 20 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

21. Natera not only developed the pivotal technology for personalized MRD testing, but has also invested considerable time and resources into developing the personalized cancer monitoring market. It has lobbied and convinced physicians, researchers, regulatory authorities and private payors on the feasibility of this new personalized cancer monitoring technology through extensive studies, which led Medicare to issue a draft Local Coverage Determination (“LCD”) for Signatera in March 2019. In its draft LCD, Medicare determined that “[t]he analytical validity and clinical validity of minimal residual disease testing using cell-free DNA, and Signatera in particular, appears to be well established based on available information for the test.”

Answer to First Amended Complaint No. 21:

Paragraph 21 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 21 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

22. In addition, Signatera[®] achieved its first commercial policy coverage by Blue Cross and Blue Shield of Louisiana, effective January 1, 2023, which covers Signatera testing for plan

members diagnosed with colorectal and muscle invasive bladder cancer and for pan-cancer immunotherapy monitoring. Additionally, effective March 1, 2023, Blue Shield of California, allows tumor-informed ctDNA testing with Signatera for patients with stage I-IV cancer to provide information for performing targeted therapy and/or monitoring for relapse or progression.

Answer to First Amended Complaint No. 22:

Paragraph 22 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 22 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

23. The clinical significance of Signatera has been acknowledged in over 40 peer-reviewed publications, including validation across multiple cancer types to detect recurrence earlier compared to standard diagnostic tools. At the American Society of Clinical Oncology (“ASCO”) Annual Meeting held from June 2–6, 2023, Natera announced its new data on Signatera across a wide variety of cancers, including colorectal (“CRC”), lung, bladder, esophageal, pancreatic, melanoma, sarcoma and cholangiocarcinoma. The results highlight the significance of Signatera among the oncology community as a platform to effectively use ctDNA to predict patient outcomes and assess treatment response for both common and rare cancers.

Answer to First Amended Complaint No. 23:

Paragraph 23 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 23 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

24. Natera continues to be a global leader in cell-free DNA testing and was recognized among the top 10 most innovative health companies of 2022 for its development of Signatera. Signatera was also a finalist of the Fierce Life Science Innovation Awards for Medical Device Innovation in 2021. Signatera also won the 2021 MedTech Breakthrough Award for “Best New Technology Solution – Biopsy” in the medical device category.

Answer to First Amended Complaint No. 24:

Paragraph 24 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 24 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

25. The Asserted Patents resulted from Natera’s years-long research in developing innovative new methods for amplifying and sequencing cell-free DNA.

Answer to First Amended Complaint No. 25:

Paragraph 25 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 25 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

General Background of the Inventions

A. The ’454 Patent

26. The ’454 Patent (Doc. 1-1) is entitled “Detecting Mutations and Ploidy in Chromosomal Segments” and issued from the USPTO on December 20, 2022. Natera owns the ’454 Patent, including the right to enforce it and seek damages for infringement.

Answer to First Amended Complaint No. 26:

NeoGenomics admits that, on its face, the ’454 Patent is entitled “Detecting Mutations and

Ploidy in Chromosomal Segments,” states that it was issued on December 20, 2022, and lists Natera as the assignee. As to the remaining allegations, NeoGenomics is without knowledge or information sufficient to form a belief as the truth of the allegations, and therefore denies the remaining allegations in that paragraph.

27. The '454 Patent claims methods for preparing plasma samples to detect ploidy of chromosome segments and SNV mutations. The claimed methods perform whole genome sequencing of tumor samples and multiplex amplification of cfDNA isolated from plasma samples in order to detect SNV mutations. Independent claim 1 of the '454 Patent recites:

A method for preparing a plasma sample of a subject having cancer or suspected of having cancer or useful for detecting one or more single nucleotide variant (SNV) mutations in the plasma sample, the method comprising:

performing whole exome sequencing or whole genome sequencing on a tumor sample of the subject to identify a plurality of tumor-specific SNV mutations;

performing targeted multiplex amplification to amplify 10 to 500 target loci each encompassing a different tumor-specific SNV mutation from cell-free DNA isolated from a plasma sample of the subject or DNA derived therefrom to obtain amplicons having a length of 50-150 bases, wherein the target loci are amplified together in the same reaction volume; and

sequencing the amplicons to obtain sequence reads, and detecting one or more of the tumor-specific SNV mutations present in the cell-free DNA from the sequence reads, wherein the sequencing has a depth of read of at least 50,000 per target locus.

Answer to First Amended Complaint No. 27:

NeoGenomics admits that, on its face, claim 1 of the '454 Patent recites:

A method for preparing a plasma sample of a subject having cancer or suspected of having cancer or useful for detecting one or more single nucleotide variant (SNV) mutations in the plasma sample, the method comprising:

performing whole exome sequencing or whole genome sequencing on a tumor sample of the subject to identify a plurality of tumor-specific SNV mutations;

performing targeted multiplex amplification to amplify 10 to 500 target loci each encompassing a different tumor-specific SNV mutation from cell-free DNA isolated from a plasma sample of the subject or DNA derived therefrom to obtain amplicons having a length of 50-150 bases, wherein the target loci are amplified together in the same reaction volume; and

sequencing the amplicons to obtain sequence reads, and detecting one or more of the tumor-specific SNV mutations present in the cell-free DNA from the sequence reads, wherein the sequencing has a depth of read of at least 50,000 per target locus.

NeoGenomics admits that claim 1 recites “single nucleotide variant (SNV) mutations,” “whole genome sequencing,” and “multiplex amplification.” NeoGenomics denies the remaining allegations in paragraph 27.

28. The claims of the '454 Patent are not directed to an abstract idea, natural law, or natural phenomenon. Rather, they are directed to an innovative method of sample preparation comprising both sequencing a tumor sample and amplifying nucleic acid samples obtained from blood plasma using synthetic primers and amplification products to provide a novel, innovative, and personalized solution to the particular problem of detecting ploidy of chromosome segments and SNVs in patients with cancer. The claims of the '454 Patent cover methods of preparation of an unnatural preparation.

Answer to First Amended Complaint No. 28:

Paragraph 28 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 28.

29. The '454 Patent claims are directed to specific, nonconventional, non-routine methods for overcoming previously unresolved problems in this area. For example, as of the date of the invention, it would not have been routine or conventional to perform the claimed techniques either individually or in combination, including: performing whole exome sequencing or whole

genome sequencing on a tumor sample to identify a plurality of tumor-specific SNV mutations, performing targeted multiplex amplification to amplify 10 to 500 target loci each encompassing a different tumor-specific SNV mutation from cfDNA to obtain amplicons having a length of 50-150 bases, wherein the target loci are amplified together in the same reaction, and sequencing the amplicons to obtain sequence reads, wherein the sequencing has a depth of read of at least 50,000 per target locus.

Answer to First Amended Complaint No. 29:

Paragraph 29 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 29.

B. The '596 Patent

30. The '596 Patent (Exhibit 1, Doc. 337-1 at 29-248), is entitled “Detecting Mutations and Ploidy in Chromosomal Segments” and issued from the USPTO on May 3, 2022. Natera owns the '596 Patent, including the right to enforce it and seek damages for infringement.

Answer to First Amended Complaint No. 30:

NeoGenomics admits that, on its face, the '596 Patent is entitled “Detecting Mutations and Ploidy in Chromosomal Segments,” states that it was issued on May 3, 2022, and lists Natera as the assignee. As to the remaining allegations, NeoGenomics is without knowledge or information sufficient to form a belief as the truth of the allegations, and therefore denies the remaining allegations in that paragraph.

31. The '596 Patent claims methods for preparing biological samples to detect ploidy of chromosome segments and single nucleotide variant (“SNV”) mutations. The claimed methods perform sequencing of tumor samples and multiplex amplification of cfDNA isolated from

biological samples in a single reaction volume in order to detect SNV mutations. Independent claim 1 of the '596 Patent recites:

A method for preparing biological samples useful for monitoring the progression of cancer in a subject, the method comprising:

- (a) performing sequencing on a tumor biopsy sample of the subject to identify a plurality of tumor-specific mutations, wherein the tumor-specific mutations comprise one or more single nucleotide variant (SNV) mutations;
- (b) evaluating results of the sequencing on the tumor biopsy sample to determine a plurality of target loci specific to the subject, wherein each target locus spans a tumor-specific mutation of the identified plurality of tumor-specific mutations; and
- (c) assaying cell-free DNA isolated from a plurality of biological samples obtained from the subject at different time points, wherein the assaying comprises:
 - performing targeted multiplex PCR amplification to amplify the plurality of target loci together in the same reaction volume from the isolated cell-free DNA using primers specific to the plurality of target loci for the individual subject; and
 - performing high-throughput sequencing of the amplified DNA comprising the plurality of target loci to obtain sequence reads, wherein an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA having the SNV locus is detected from the sequence reads.

Answer to First Amended Complaint No. 31:

NeoGenomics admits that, on its face, claim 1 of the '596 Patent recites:

A method for preparing biological samples useful for monitoring the progression of cancer in a subject, the method comprising:

- (d) performing sequencing on a tumor biopsy sample of the subject to identify a plurality of tumor-specific mutations, wherein the tumor-specific mutations comprise one or more single nucleotide variant (SNV) mutations;
- (e) evaluating results of the sequencing on the tumor biopsy sample to determine a plurality of target loci specific to the subject, wherein each target locus spans a tumor-specific mutation of the identified plurality of tumor-specific

mutations; and

- (f) assaying cell-free DNA isolated from a plurality of biological samples obtained from the subject at different time points, wherein the assaying comprises:

performing targeted multiplex PCR amplification to amplify the plurality of target loci together in the same reaction volume from the isolated cell-free DNA using primers specific to the plurality of target loci for the individual subject; and

performing high-throughput sequencing of the amplified DNA comprising the plurality of target loci to obtain sequence reads, wherein an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA having the SNV locus is detected from the sequence reads.

NeoGenomics admits that claim 1 recites “sequencing on a tumor biopsy sample,” “performing targeted multiplex PCR amplification . . . in the same reaction volume from the isolated cell-free DNA,” and “ having the SNV locus [] detected.” NeoGenomics denies the remaining allegations in paragraph 31.

32. The claims of the '596 Patent are not directed to an abstract idea, natural law, or natural phenomenon. Rather, they are directed to an innovative method of sample preparation comprising both sequencing a tumor sample and amplifying nucleic acid samples obtained from blood plasma using synthetic primers and amplification products to provide a novel, innovative, and personalized solution to the particular problem of detecting ploidy of chromosome segments and SNVs in patients with cancer. The claims of the '596 Patent cover methods of preparation of an unnatural preparation.

Answer to First Amended Complaint No. 32:

Paragraph 32 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 32.

33. The '596 Patent claims are directed to specific, nonconventional, non-routine methods for overcoming previously unresolved problems in this area. For example, as of the date of the invention, it would not have been routine or conventional to perform the claimed techniques either individually or in combination, including: performing sequencing on a tumor sample, evaluating results of the sequencing to determine a plurality of target loci wherein each target locus spans a tumor-specific mutation, assaying cfDNA isolated from a plurality of biological samples obtained from a subject at different time points wherein the assaying includes (i) performing targeted multiplex amplification to amplify the plurality of target loci on isolated cfDNA in the same reaction, and (ii) performing high-throughput sequencing of the amplified DNA to obtain sequence reads, wherein an SNV mutation that is present in less than or equal to 0.015% of the cfDNA having the SNV locus is detected from the sequence reads.

Answer to First Amended Complaint No. 33:

Paragraph 33 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 33.

DEFENDANT'S INFRINGING ACTS

34. The allegations provided below are exemplary and without prejudice to Natera's infringement contentions. In providing these allegations, Natera does not convey or imply any particular claim constructions or the precise scope of the claims. Natera's claim construction contentions regarding the meaning and scope of the claim terms will be provided under the Court's scheduling order and local rules.

Answer to First Amended Complaint No. 34:

Paragraph 34 of the Amended Complaint purports to contain disclaimers and provisos by Natera to which no response is required. To the extent a response is required, NeoGenomics denies

each and every allegation in paragraph 34.

35. The infringing products include, but are not limited to, RaDaR, and any other infringing method, product, device, or test developed by Defendant that apply Natera's patented methods for preparing, amplifying, sequencing, and analyzing cfDNA to detect and monitor genes and genetic mutations associated with a patient's cancer.

Answer to First Amended Complaint No. 35:

NeoGenomics denies that any of its products, such as RaDaR, "apply Natera's patented methods for preparing, amplifying, sequencing, and analyzing cfDNA to detect and monitor genes and genetic mutations associated with a patient's cancer." NeoGenomics denies each and every allegation in paragraph 35.

36. As provided in more detail below, each element of at least one claim of the '454 Patent is literally present in RaDaR or is literally practiced by the processes through which RaDaR is practiced. To the extent that any element is not literally present or practiced, each such element is present or practiced under the doctrine of equivalents.

Answer to First Amended Complaint No. 36:

Paragraph 36 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 36.

37. As provided in more detail below, each element of at least one claim of the '596 Patent is literally present in RaDaR or is literally practiced by the processes through which RaDaR is practiced. To the extent that any element is not literally present or practiced, each such element is present or practiced under the doctrine of equivalents.

Answer to First Amended Complaint No. 37:

Paragraph 37 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 37.

38. Exhibits 2-3 (Doc. 337-1 at 249-489) are preliminary and exemplary claim charts describing infringement the claims of the '454 Patent and the '596 Patent, respectively. The claim charts are not intended to limit Natera's right to modify the charts or allege that other products or activities of Defendant infringe the identified claims or any other claims of the Asserted Patents or any other patents. Defendant infringes more than one claim of the '454 Patent and infringes more than one claim of the '596 Patent.

Answer to First Amended Complaint No. 38:

NeoGenomics admits that documents purporting to be claim charts for the claims of the '454 Patent and the '596 Patent are attached to the Complaint as Exhibits 2–3. The claim charts contain statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in the claim charts. NeoGenomics denies each and every allegation in paragraph 38.

39. Exhibits 2-3 are hereby incorporated by reference in their entirety. Each claim element in Exhibit 2 that is mapped to the Accused Assay shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure, and therefore a response to each claim element is required. Each claim element in Exhibit 3 that is mapped to the Accused Assay shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure, and therefore a response to each claim element is required.

Answer to First Amended Complaint No. 39:

Paragraph 39 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in Exhibit 2 and Exhibit 3. NeoGenomics further denies each and every allegation in paragraph 39.

40. Upon information and belief, NeoGenomics Laboratories designs, develops, makes and uses, or directs or controls the design, development, make and use of, the RaDaR assay by purposefully directing the activities at its CAP/CLIA-certified laboratory in the Research Triangle Park (RTP) located at 8 Davis Drive, Durham, North Carolina. According to the CAP and CLIA certificates, this laboratory is registered to Inivata, Inc., a corporate affiliate of NeoGenomics Laboratories, and the director of this laboratory is Dr. Siby Sebastian, Ph.D. On its website, NeoGenomics Laboratories acknowledges that Dr. Siby Sebastian is also “the Director of the NeoGenomics CAP/CLIA Clinical Laboratory at the Research Triangle Park (RTP), North Carolina.” Moreover, according to its 2022 Annual Report to shareholders (Doc. 1-21), NeoGenomics Laboratories stated that “[w]e have a renewed focus on next-generation sequencing (NGS), minimal residual disease (MRD) technology such as RaDaR . . . By centralizing the R&D function and integrating Inivata, we believe we are now well-positioned to capitalize on the innovation of Inivata while enhancing the development process for new product.”

Answer to First Amended Complaint No. 40:

NeoGenomics admits that it “designs, develops, makes and uses, or directs or controls the design, development, make and use of” parts of the RaDaR assay by “purposefully directing the activities at its CAP/CLIA-certified laboratory in the Research Triangle Park (RTP)” located at 5 Triangle Drive, Durham, North Carolina. NeoGenomics further admits that this laboratory is

registered to NeoGenomics Laboratories. NeoGenomics admits that Dr. Siby Sebastian, Ph.D previously served as a director of this laboratory. NeoGenomics further admits that Dr. Siby Sebastian was “the Director of the NeoGenomics CAP/CLIA Clinical Laboratory at the Research Triangle Park (RTP), North Carolina.” NeoGenomics further admits that the laboratory previously located at 8 Davis Drive, Durham, North Carolina is no longer in use. NeoGenomics admits that it “designs, develops, makes and uses, or directs or controls the design, development, make and use of” the bioinformatics of the RaDaR assay outside the United States. NeoGenomics admits that its 2022 Annual Report to shareholders indicated NeoGenomics “ha[s] a renewed focus on next-generation sequencing (NGS), minimal residual disease (MRD) technology such as RaDaR®, MultiOmyx™, and data capture and commercialization. Functions under this business include Pharma Services, as it is the tip of the spear for driving innovation in our industry, Informatics (the former Trapelo business), and centralized research and development. By centralizing the R&D function and integrating Inivata, we believe we are now well-positioned to capitalize on the innovation of Inivata while enhancing the development process for new products.”

41. On December 27, 2023, the only commercially available version of NeoGenomics Laboratories’ RaDaR assay (“RaDaR 1.0”) was preliminary enjoined.

Answer to First Amended Complaint No. 41:

NeoGenomics admits that, on December 27, 2023, the Court issued an order (Doc. 171) granting Natera’s Motion for a Preliminary Injunction to enjoin NeoGenomics from “(1) making, using, selling, or offering for sale in the United States (a) the accused RaDaR [1.0] assay (“the Accused Assay”) or (b) any assay or product not more than colorably different from the Accused Assay whose manufacture, use, importation, offer for sale, or sale would infringe any asserted claim of U.S. Patent No. 11,519,035.” The Court further ordered, “NeoGenomics may continue

to make, use, and sell [RaDaR 1.0 assay] solely for continued use of [RaDaR 1.0 assay] a. for those patients already using it before the entry of this injunction, b. in support of research and development with other persons or entities on projects or studies that began before the entry of this injunction, or c. for use in or in support of clinical trials in process or already approved by an agency of the United States.” (Doc. 171.)

42. NeoGenomics Laboratories “agreed, for the purposes of [a] Permanent Permanent Injunction, not to contest that (a) NeoGenomics infringed Claims 1, 2, 12, and 13 of U.S. Patent No. 11,519,035 and Claims 1-28 of U.S. Patent No. 11,530,454 (“the Asserted Claims”) by making, offering for sale, and selling the accused RaDaR 1.0 assay and (b) the Asserted Claims are valid and enforceable.” On September 23, 2024, the preliminarily enjoined RaDaR assay and any assay not more than colorably different were permanently enjoined.

Answer to First Amended Complaint No. 42:

NeoGenomics admits that as a part of a Confidential Settlement Agreement executed on September 20, 2024, NeoGenomics “agreed, for purposes of [a] Stipulated Permanent Injunction, not to contest that (a) NeoGenomics infringed Claims 1, 2, 12, and 13 of U.S. Patent No. 11,519,035 and Claims 1-28 of U.S. Patent No. 11,530,454 (“the Asserted Claims”) by making, offering for sale, and selling the accused RaDaR 1.0 assay and (b) the Asserted Claims are valid and enforceable.” (Doc. 329.) NeoGenomics also admits that, on December 27, 2023, the Court issued an order (Doc. 171) granting Natera’s Motion for a Preliminary Injunction to enjoin NeoGenomics from “(1) making, using, selling, or offering for sale in the United States (a) the accused RaDaR [1.0] assay (“the Accused Assay”) or (b) any assay or product not more than colorably different from the Accused Assay whose manufacture, use, importation, offer for sale, or sale would infringe any asserted claim of U.S. Patent No. 11,519,035.” The Court further

ordered, “NeoGenomics may continue to make, use, and sell [RaDaR 1.0 assay] solely for continued use of [RaDaR 1.0 assay] a. for those patients already using it before the entry of this injunction, b. in support of research and development with other persons or entities on projects or studies that began before the entry of this injunction, or c. for use in or in support of clinical trials in process or already approved by an agency of the United States.” (Doc. 171.)

43. Upon information and belief, after the preliminary injunction issued, NeoGenomics Laboratories began working on a modified version of the RaDaR assay. Upon information and belief, NeoGenomics Laboratories refers to this modified version of RaDaR as “RaDaR 1.1.”

Answer to First Amended Complaint No. 43:

Admitted.

44. Upon information and belief, NeoGenomics Laboratories entered the feasibility stage of assay development in March 2024 for “RaDaR 1.1.”

Answer to First Amended Complaint No. 44:

NeoGenomics admits that starting in March 2024, it began the feasibility stage of assay development for RaDaR 1.1.

45. Upon information and belief, NeoGenomics Laboratories performs, or directs or controls the performance of, the RaDaR assay. In its published guide for patients, NeoGenomics Laboratories states that RaDaR testing is “conducted on [a] blood sample in our lab.”

Answer to First Amended Complaint No. 45:

NeoGenomics admits that it performs, or directs or controls the performance of, the RaDaR assay. NeoGenomics further admits that, in its published guide for patients, NeoGenomics Laboratories states that RaDaR testing is “conducted on [a] blood sample in our lab.”

46. On March 16, 2023, NeoGenomics began selling and offering to sell RaDaR 1.0 in the United States. Upon information and belief, NeoGenomics Laboratories offers for sale and sells, or directs or controls the offer for sale and sale of, RaDaR 1.0 “for those patients already using it before the Preliminary Injunction issued on January 10, 2024, including for patients who had blood samples taken before January 10, 2024 and on samples taken thereafter for those same patients.”

Answer to First Amended Complaint No. 46:

NeoGenomics admits that, on March 16, 2023, it launched the RaDaR 1.0 product for sale in clinical settings in the United States. NeoGenomics admits that, on April 23, 2020, it launched the RaDaR 1.0 product for sale for research use in the United States. NeoGenomics also admits that it “continue[s] to make, use, and sell” RaDaR 1.0 “a. for those patients already using it before the Preliminary Injunction issued on January 10, 2024, including for patients who had blood samples taken before January 10, 2024 and on samples taken thereafter for those same patients; b. in support of research and development with other persons or entities on projects or studies that began before January 10, 2024; or c. for use in or in support of clinical trials that were in process or already approved by an agency of the United States before January 10, 2024, including three trials for which NeoGenomics had signed contracts as of January 10, 2024 but testing had not yet begun at that time, and also including three additional trials identified in Docket 206 where contracts had not yet been finalized as of January 10, 2024.” (Doc. 329.)

47. In its 2022 Annual Report to shareholders, NeoGenomics Laboratories stated that “[w]e believe NeoGenomics is well-positioned to gain market share with our . . . RaDaR® assay liquid biopsy test for MRD.”

Answer to First Amended Complaint No. 47:

NeoGenomics admits that, in its 2022 Annual Report to shareholders, it stated that “[w]e believe NeoGenomics is well-positioned to gain market share with our NGS portfolio products, including Neo Comprehensive – Solid Tumor and Neo Comprehensive – Myeloid Disorders, as well as our RaDaR® assay liquid biopsy test for MRD.”

48. Upon information and belief, NeoGenomics Laboratories intends to offer for sale and intends to sell, or intends to direct or control the offer for sale and sale of, RaDaR 1.1.

Answer to First Amended Complaint No. 48:

NeoGenomics admits that it currently intends to offer for sale, sell, or direct or control the offer for sale and sale of, RaDaR 1.1 once RaDaR 1.1 has been validated. NeoGenomics’ intentions are subject to the ongoing development and testing of RaDaR 1.1.

49. Upon information and belief, NeoGenomics Laboratories induces Inivata to perform any RaDaR tests that NeoGenomics is not performing itself. While RaDaR is ordered through NeoGenomics Laboratories, its insurance reimbursement certifications and approvals, including MolDX, list Inivata as authorized to perform RaDaR tests. In addition, the request forms for the RaDaR test report that RaDaR may be performed by Inivata.

Answer to First Amended Complaint No. 49:

NeoGenomics admits that RaDaR is ordered through NeoGenomics Laboratories, but its insurance reimbursement certifications and approvals, including MolDX, list Inivata as authorized to perform RaDaR tests. NeoGenomics further admits that the request forms for the RaDaR test report that RaDaR may be performed by Inivata. Paragraph 49 otherwise contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 49.

50. NeoGenomics Laboratories is a direct competitor of Natera in the market for personalized, tumor-informed recurrence monitoring specifically. In promoting its infringing RaDaR assay, NeoGenomics Laboratories repeatedly undermined Signatera and Natera to investors, including at the Goldman Sachs 44th Annual Global Healthcare Conference held on June 13, 2023. NeoGenomics Laboratories touted its infringing and competing RaDaR assay to investors as being “about 10x more sensitive than the other product that’s really commercially available in the market,” which is Signatera, even though there is no clinical evidence or head-to-head study to substantiate this claim. On information and belief, representatives of NeoGenomics Laboratories have repeated similar misleading claims to potential customers, including current Signatera customers, in promoting the infringing RaDaR assay.

Answer to First Amended Complaint No. 50:

Paragraph 50 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 50.

51. On July 27, 2023, NeoGenomics Laboratories announced that RaDaR 1.0 obtained Medicare coverage for cancer recurrence detection and monitoring in patients with breast cancer.

Answer to First Amended Complaint No. 51:

NeoGenomics admits that, on July 27, 2023, it announced that RaDaR obtained Medicare coverage for cancer recurrence detection and monitoring in patients with breast cancer, including those with a personal history of high-risk stage II/III HR+/HER2- breast cancer, five or more years from diagnosis who presently do not have evidence of disease.

52. NeoGenomics Laboratories has actual knowledge of the ’454 Patent since at least as early as December 20, 2022, when Natera filed an infringement lawsuit in the District of

Delaware asserting the '454 Patent against two corporate affiliates of NeoGenomics Laboratories: Inivata, Inc., and Inivata, Ltd.

Answer to First Amended Complaint No. 52:

NeoGenomics admits that it had actual knowledge of the '454 Patent since at least as early as December 20, 2022 when Natera filed an infringement lawsuit in the District of Delaware asserting the '454 Patent against two corporate affiliates of NeoGenomics Laboratories, Inc.: Inivata, Inc., and Inivata, Ltd.

53. NeoGenomics Laboratories has actual knowledge of the '596 Patent since at least as early as the date of this First Amended Complaint.

Answer to First Amended Complaint No. 53:

NeoGenomics admits that it had actual knowledge of the '596 Patent since at least as early as the date of this First Amended Complaint.

54. NeoGenomics Laboratories has thus made extensive unauthorized use of Natera's patented technology, including the technology described and claimed in the Asserted Patents, causing Natera to suffer immediate and irreparable harm. Natera brings this action to enforce its patents rights. Natera thus requests that this Court award it damages sufficient to compensate for NeoGenomics Laboratories' infringement of the Asserted Patents, find this case exceptional, award Natera its attorneys' fees and costs, and grant an injunction against NeoGenomics Laboratories to prevent any further infringement of the Asserted Patents.

Answer to First Amended Complaint No. 54:

NeoGenomics denies that it has "made extensive unauthorized use of Natera's patented technology." The remainder of paragraph 54 of the Amended Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is

required, NeoGenomics denies each and every allegation in paragraph 54.

COUNT I: DIRECT INFRINGEMENT OF U.S. PATENT NO. 11,530,454

55. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

Answer to First Amended Complaint No. 55:

NeoGenomics incorporates and restates by reference its responses to paragraphs 1–54 of the Amended Complaint as though fully set forth herein.

56. Natera is the owner of the '454 Patent, which was duly and legally issued by the USPTO on December 20, 2022.

Answer to First Amended Complaint No. 56:

NeoGenomics lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 56 and on that basis denies them.

57. Defendant has infringed and continues to infringe at least one claim of the '454 Patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by performing, or directing or controlling the performance of, the Accused Assay within the United States and without authority.

Answer to First Amended Complaint No. 57:

NeoGenomics denies each and every allegation in paragraph 57 of the Amended Complaint.

58. Defendant's infringement has damaged and will continue to damage Natera, which is entitled to recover the damages resulting from Defendant's wrongful acts in an amount to be determined at trial, and in any event no less than a reasonable royalty.

Answer to First Amended Complaint No. 58:

NeoGenomics denies each and every allegation in paragraph 58 of the Amended Complaint.

59. Moreover, Defendant's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless Defendant, including its corporate affiliates and subsidiaries, is enjoined from any and all activities that would infringe the claims of the '454 Patent.

Answer to First Amended Complaint No. 59:

NeoGenomics denies each and every allegation in paragraph 59 of the Amended Complaint.

COUNT II: DIRECT INFRINGEMENT OF U.S. PATENT NO. 11,519,596

60. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

Answer to First Amended Complaint No. 60:

NeoGenomics incorporates and restates by reference its responses to paragraphs 1–59 of the Amended Complaint as though fully set forth herein.

61. Natera is the owner of the '596 Patent, which was duly and legally issued by the USPTO on May 3, 2022.

Answer to First Amended Complaint No. 61:

NeoGenomics lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 61 and on that basis denies them.

62. Defendant has infringed and continues to infringe at least one claim of the '596 Patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by performing,

or directing or controlling the performance of, the Accused Assay within the United States and without authority.

Answer to First Amended Complaint No. 62:

NeoGenomics denies each and every allegation in paragraph 62 of the Amended Complaint.

63. Defendant's infringement has damaged and will continue to damage Natera, which is entitled to recover the damages resulting from Defendant's wrongful acts in an amount to be determined at trial, and in any event no less than a reasonable royalty.

Answer to First Amended Complaint No. 63:

NeoGenomics denies each and every allegation in paragraph 63 of the Amended Complaint.

64. Moreover, Defendant's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless Defendant, including its corporate affiliates and subsidiaries, is enjoined from any and all activities that would infringe the claims of the '596 Patent.

Answer to First Amended Complaint No. 64:

NeoGenomics denies each and every allegation in paragraph 64 of the Amended Complaint.

COUNT III: INDIRECT INFRINGEMENT OF U.S. PATENT NO. 11,530,454

65. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

Answer to First Amended Complaint No. 65:

NeoGenomics incorporates and restates by reference its responses to paragraphs 1–59 of the Amended Complaint as though fully set forth herein.

66. NeoGenomics Laboratories has indirectly infringed and continues to indirectly infringe at least one claim of the '454 Patent pursuant to 35 U.S.C. § 271(b), literally or under the doctrine of equivalents, by inducing its corporate affiliate Inivata to perform the Accused Assay within the United States without authority. NeoGenomics Laboratories engaged in such inducement having knowledge of the '454 Patent at least as of December 20, 2022 when Natera filed a lawsuit alleging infringement of the '454 Patent by Inivata in the District of Delaware. Furthermore, NeoGenomics Laboratories knows or should know that its actions of selling or offering to sell the Accused Assay will induce direct infringement by Inivata and intends that its actions will induce direct infringement by Inivata. NeoGenomics Laboratories intends to offer for sale the Accused Assay specifically intending that Inivata perform the Accused Assay in NeoGenomics Laboratories' CAP/CLIA-certified laboratory in Durham, North Carolina upon purchase by a customer.

Answer to First Amended Complaint No. 66:

NeoGenomics denies each and every allegation in paragraph 66 of the Amended Complaint.

67. As a direct and proximate result of NeoGenomics Laboratories' indirect infringement by inducement of the '454 Patent, Natera has been and continues to be damaged. Thus, Natera is entitled to recover the damages resulting from NeoGenomics Laboratories' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonable royalty.

Answer to First Amended Complaint No. 67:

NeoGenomics denies each and every allegation in paragraph 67 of the Amended Complaint.

68. Moreover, Defendant's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless NeoGenomics Laboratories is enjoined from any and all activities that would infringe the claims of the '454 Patent.

Answer to First Amended Complaint No. 68:

NeoGenomics denies each and every allegation in paragraph 68 of the Amended Complaint.

COUNT IV: INDIRECT INFRINGEMENT OF U.S. PATENT NO. 11,319,596

69. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

Answer to First Amended Complaint No. 69:

NeoGenomics incorporates and restates by reference its responses to paragraphs 1–59 of the Amended Complaint as though fully set forth herein.

70. NeoGenomics Laboratories has indirectly infringed and continues to indirectly infringe at least one claim of the '596 Patent pursuant to 35 U.S.C. § 271(b), literally or under the doctrine of equivalents, by inducing its corporate affiliate Inivata to perform the Accused Assay within the United States without authority. NeoGenomics Laboratories engaged in such inducement having knowledge of the '596 Patent, at least as of the service of the present First Amended Complaint. Furthermore, NeoGenomics Laboratories knows or should know that its actions of selling or offering to sell the Accused Assay will induce direct infringement by Inivata and intends that its actions will induce direct infringement by Inivata. NeoGenomics Laboratories intends to offer for sale the Accused Assay specifically intending that Inivata perform the Accused Assay in NeoGenomics Laboratories' CAP/CLIA-certified laboratory in Durham, North Carolina upon purchase by a customer.

Answer to First Amended Complaint No. 70:

NeoGenomics denies each and every allegation in paragraph 70 of the Amended Complaint.

71. As a direct and proximate result of NeoGenomics Laboratories' indirect infringement by inducement of the '596 Patent, Natera has been and continues to be damaged. Thus, Natera is entitled to recover the damages resulting from NeoGenomics Laboratories' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonable royalty.

Answer to First Amended Complaint No. 71:

NeoGenomics denies each and every allegation in paragraph 71 of the Amended Complaint.

72. Moreover, Defendant's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless NeoGenomics Laboratories is enjoined from any and all activities that would infringe the claims of the '596 Patent.

Answer to First Amended Complaint No. 72:

NeoGenomics denies each and every allegation in paragraph 72 of the Amended Complaint.

COUNT V: WILLFUL INFRINGEMENT OF U.S. PATENT NO. 11,530,454

73. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

Answer to First Amended Complaint No. 73:

NeoGenomics incorporates and restates by reference its responses to paragraphs 1–59 of the Amended Complaint as though fully set forth herein.

74. NeoGenomics Laboratories has acted willfully and egregiously in performing the acts of infringement identified in this First Amended Complaint. NeoGenomics Laboratories' infringement of the '454 Patent has been and is deliberate and willful and constitutes egregious misconduct. NeoGenomics Laboratories engaged in such conduct having knowledge of the '454 Patent at least as of December 20, 2022 when Natera filed a lawsuit alleging infringement of the '454 Patent by Inivata in the District of Delaware. Furthermore, NeoGenomics Laboratories knows or should know that its actions, including its actions of selling or offering to sell the Accused Assay, will induce direct infringement by Inivata and intends that its actions will induce direct infringement by Inivata. NeoGenomics Laboratories intends to offer for sale the Accused Assay specifically intending that Inivata perform the Accused Assay in NeoGenomics Laboratories' CAP/CLIA-certified laboratory in Durham, North Carolina upon purchase by a customer. In performing the acts of infringement identified in this First Amended Complaint, NeoGenomics Laboratories has been willfully blind to its ongoing infringement.

Answer to First Amended Complaint No. 74:

NeoGenomics denies each and every allegation in paragraph 74 of the Amended Complaint.

75. As a direct and proximate result of NeoGenomics Laboratories' willful infringement, Natera has been and continues to be damaged. Thus, Natera is entitled to recover the damages resulting from NeoGenomics Laboratories' wrongful acts in an amount to be determined at trial. Natera deserves treble damages and the reimbursement of its fees and costs as set forth in 35 U.S.C. §§ 284 and 285.

Answer to First Amended Complaint No. 75:

NeoGenomics denies each and every allegation in paragraph 75 of the Amended

Complaint.

76. Moreover, Defendant's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless NeoGenomics Laboratories is enjoined from any and all activities that would infringe the claims of the '454 Patent.

Answer to First Amended Complaint No. 76:

NeoGenomics denies each and every allegation in paragraph 76 of the Amended Complaint.

COUNT VI: WILLFUL INFRINGEMENT OF U.S. PATENT NO. 11,319,596

77. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

Answer to First Amended Complaint No. 77:

NeoGenomics incorporates and restates by reference its responses to paragraphs 1–59 of the Amended Complaint as though fully set forth herein.

78. NeoGenomics Laboratories has acted willfully and egregiously in performing the acts of infringement identified in this First Amended Complaint. NeoGenomics Laboratories' infringement of the '596 Patent has been and is deliberate and willful and constitutes egregious misconduct. NeoGenomics Laboratories engaged in such conduct having knowledge of the '596 Patent, at least as of the service of the present First Amended Complaint. Furthermore, NeoGenomics Laboratories knows or should know that its actions, including its actions of selling or offering to sell the Accused Assay, will induce direct infringement by Inivata and intends that its actions will induce direct infringement by Inivata. NeoGenomics Laboratories intends to offer for sale the Accused Assay specifically intending that Inivata perform the Accused Assay in NeoGenomics Laboratories' CAP/CLIA-certified laboratory in Durham, North Carolina upon

purchase by a customer. In performing the acts of infringement identified in this First Amended Complaint, NeoGenomics Laboratories has been willfully blind to its ongoing infringement.

Answer to First Amended Complaint No. 78:

NeoGenomics denies each and every allegation in paragraph 78 of the Amended Complaint.

79. As a direct and proximate result of NeoGenomics Laboratories' willful infringement, Natera has been and continues to be damaged. Thus, Natera is entitled to recover the damages resulting from NeoGenomics Laboratories' wrongful acts in an amount to be determined at trial. Natera deserves treble damages and the reimbursement of its fees and costs as set forth in 35 U.S.C. §§ 284 and 285.

Answer to First Amended Complaint No. 79:

NeoGenomics denies each and every allegation in paragraph 79 of the Amended Complaint.

80. Moreover, Defendant's infringement has caused, and will continue to cause, irreparable injury to Natera, for which damages are an inadequate remedy, unless NeoGenomics Laboratories is enjoined from any and all activities that would infringe the claims of the '596 Patent.

Answer to First Amended Complaint No. 80:

NeoGenomics denies each and every allegation in paragraph 80 of the Amended Complaint.

PRAYER FOR RELIEF

NeoGenomics denies that Natera is entitled to any relief whatsoever, including the relief requested in the Amended Complaint, from either NeoGenomics or the Court. Natera's prayer for relief should be denied in its entirety.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, NeoGenomics respectfully demands a trial by jury on all triable issues.

AFFIRMATIVE DEFENSES

NeoGenomics hereby sets forth defenses to Natera's Amended Complaint in order to place Natera on notice regarding applicable defenses. By listing any matter as a defense herein, NeoGenomics does not assume the burden of proving any matter upon which Natera, or any other party, bears the burden of proof under applicable law.

FIRST DEFENSE – NON-INFRINGEMENT

1. NeoGenomics has not infringed, and is not infringing directly, indirectly, willfully, or in any other manner any valid and enforceable claim of the Asserted Patents, either literally or under the doctrine of equivalents.

2. NeoGenomics hereby incorporates by reference its response to Natera's interrogatory No. 4 and any supplements and amendments thereof.

3. By way of example, first, NeoGenomics does not infringe claim 1 of the '454 Patent or its dependents because NeoGenomics does not perform targeted multiplex amplification to obtain amplicons having a length of 50-150 bases. Second, NeoGenomics does not infringe any claims of the '454 Patent because NeoGenomics's RaDaR Assay does not sequence the amplicons obtained from the claimed targeted multiplex amplification step, but includes intervening steps between multiplex amplification and sequencing the products. Third, NeoGenomics does not infringe any claims of the '454 Patent because NeoGenomics's RaDaR Assay does not perform sequencing and detecting as "part of one sequencing step" as required by the claim language as construed by the Court. Fourth, NeoGenomics does not infringe any claims of the '454 Patent because NeoGenomics' RaDaR Assay does not perform all claimed steps in the United States.

Fifth, NeoGenomics does not infringe claim 14 of the '454 Patent or its dependents because NeoGenomics' RaDaR Assay is not capable of detecting an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA having the SNV locus. Sixth, NeoGenomics does not infringe claims 1-13 and 15 of the '454 Patent because NeoGenomics' RaDaR Assay does not perform sequencing wherein the sequencing has a depth of read of at least 50,000 per target locus.

4. By way of example, NeoGenomics does not infringe any claims of the '596 Patent because NeoGenomics' RaDaR Assay does not detect from the sequence reads an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA having the SNV locus. NeoGenomics also does not infringe any claims of the '596 Patent because NeoGenomics' RaDaR Assay does not perform all claimed steps in the United States.

SECOND DEFENSE – INVALIDITY

5. The asserted claims of the Asserted Patents are invalid for failing to comply with one or more of the requirements for patentability under, including, but not limited to, 35 U.S.C. §§ 101, 102, 103, 112 *et seq.*, and the rules, regulations, and laws pertaining to those provisions, including the application provisions of Title 37 of the Code of Federal Regulations.

6. NeoGenomics hereby incorporates by reference in their entirety its invalidity contentions served on February 23, 2024, July 11, 2024 and December 18, 2024, Dr. Niall Lennon's opening expert report served on August 2, 2024, and its Petition for *Inter Partes* Review of U.S. Patent No. 11,530,454 filed on December 19, 2023, and any prior art referenced therein.

7. By way of example, the asserted claims are invalid as obvious under Forshew et al., “*Noninvasive Identification and Monitoring of Cancer Mutations by Targeted Deep Sequencing of Plasma DNA*,” Sci Transl Med 4, 136ra68 (2012) (including Supplementary Materials available at www.sciencetranslationalmedicine.org/cgi/content/full/4/136/136ra68/DC1) (“Forshew (2012)”).

and the skill and knowledge of a person of ordinary skill in the art at the alleged time of the invention of the Asserted Patents. Further, the asserted claims are directed to patent-ineligible subject matter, namely, that they are directed to a method of detection claim that recites nothing more than an abstract, mental process implemented with a mathematical algorithm.

8. By way of example, the asserted claims are invalid for lack of written description. Asserted claims from both patents contain terms with no support in the specification, demonstrating that the inventors did not have possession of the invention.

THIRD DEFENSE – FAILURE TO STATE A CLAIM

9. Natera's Amended Complaint, in whole or in part, fails to state a claim upon which relief may be granted.

10. As an example, Natera's Amended Complaint fails to state a claim upon which relief may be granted because the claims of the Asserted Patents are invalid for failing to comply with one or more of the requirements for patentability under, including, but not limited to, 35 U.S.C. §§ 101, 102, 103, 112 *et seq.* as set forth below in NeoGenomics' Counterclaims.

11. NeoGenomics hereby incorporates by reference and restates Paragraphs 1-9 of its Affirmative Defenses as though fully set forth herein.

FOURTH DEFENSE – PROSECUTION HISTORY ESTOPPEL/DISCLAIMER

12. Natera is estopped from construing the claims of the Asserted Patents to cover or include, either literally or by application of the doctrine of equivalents, products manufactured, used, imported, sold, or offered for sale by NeoGenomics or methods used by NeoGenomics because of amendments, admissions, representations, or statements made before the USPTO during prosecution of the applications leading to the issuance of the Asserted Patents or applications related thereto, because of disclosures or language in the specifications of the Asserted Patents, and/or because of limitations in the claims of the Asserted Patents.

13. By way of example, Natera asserted to the USPTO during the prosecution of related U.S. Patent No. 11,486,008, that its alleged invention involved “performing high-throughput sequencing to **sequence the amplicons obtained in the multiplex targeted amplification reaction** to obtain sequence reads.” Natera further asserted that “[i]n contrast to the claimed invention, Forshew’s TAM-Seq process requires a ‘*limited-cycle pre-amplification step*’ followed by ‘*individual amplification to purify and select for intended targets*’ (i.e., parallel single-plex PCR).” As another example, Natera asserted to the PTAB in response to the petition for IPR against the ’454 Patent that Forshew “plainly did consider and reject use of multiplex amplification alone,” leading the PTAB to deny institution of the IPR petition because Forshew “only referred to the single-plex amplification products as amplicons to be sequenced.”

14. The assertions that Natera has made in order to overcome the prior art show that the Asserted Claims require that the sequencing be performed on the amplicons obtained from the multiplex targeted amplification reaction, not the amplicons obtained from some other intervening step.

15. Because of these assertions, Natera is now estopped from construing the claims of the claims of the ’454 Patent or the ’596 Patent to cover or include, either literally or by application of the doctrine of equivalents, products manufactured, used, imported, sold, or offered for sale by NeoGenomics or methods used by NeoGenomics.

FIFTH DEFENSE – LIMITATIONS ON RECOVERY

16. Natera’s claims for damages and other remedies are limited by 35 U.S.C. §§ 287 and/or 288. Natera is barred by 35 U.S.C. § 288 from recovering costs associated with this action.

SIXTH DEFENSE – ADEQUATE REMEDY AT LAW

17. Natera is not entitled to injunctive relief against NeoGenomics because Natera is not likely to succeed on the merits, any alleged injury is neither immediate nor irreparable, there

is an adequate remedy at law for any alleged injury, the balance of hardships and equities does not favor an injunction, and the public interest would be disserved by an injunction. Accordingly, Natera is not entitled to injunctive relief even if it were able to establish liability.

SEVENTH DEFENSE – NO EXCEPTIONAL CASE

18. NeoGenomics has not engaged in any conduct that would make this an exceptional case or that would entitle Natera to an award of attorneys' fees.

EIGHTH DEFENSE – ACTIONS OF OTHERS

19. On information and belief, Natera's claims are barred, in whole or in part, because NeoGenomics is not liable for the acts of others over whom it has no control.

NINTH DEFENSE – IMPROPER INVENTORSHIP

20. The '454 Patent and '596 Patents are invalid under at least 35 U.S.C. §§ 101, 115, 116, 256, and/or any judicially created doctrine of invalidity, including improper inventorship, for failing to name the correct inventors of the claimed invention. The '454 Patent and '596 Patents each list Joshua Babiarz, Tudor Pompiliu Constantin, Lane A. Eubank, Goerge Gemelos, Matthew Micah Hill, Huseyin Eser Kirkizlar, Matthew Rabinowitz, Onur Sakarya, Styrmir Sigurjonsson, and Bernhard Zimmerman from Natera as inventors. However, aspects of the '454 Patent and '596 Patent, including the detection and determination of clonal and/or subclonal single nucleotide variant ("SNV") mutations, were in fact conceived and reduced to practice by researchers at University College London ("UCL"), including at least Drs. Mariam Jamal-Hanjani and Charles Swanton, as part of the TRACERx (TRAcking Cancer Evolution through therapy (Rx)) study.

21. The '454 Patent claims methods of preparing a plasma sample for detecting "clonal SNV mutations" and/or "subclonal SNV mutations," as well as "determining clonal heterogeneity

of the tumor sample” present in “cell-free DNA isolated from a plasma sample.” On information and belief, researchers at UCL, including at least Drs. Mariam Jamal-Hanjani and Charles Swanton, conceived, reduced to practice, and communicated these claimed methods to the named inventors of the ’454 Patent.

22. Similarly, the ’596 Patent claims methods of preparing a plasma sample for detecting “clonal SNV mutations” and/or “subclonal SNV mutations.” The ’596 Patent specifically claims clonal SNV mutations such as “CYFIP1, FAT1, MLLT4, RASA1, HERC4, JAK2, MSH2, MTOR, PLCG2, GARRG1, and TRIM67.” The ’596 Patent also specifically claims subclonal SNV mutations such as “CIC, KDM6A, NF1, and TRIM67.” On information and belief, researchers at UCL, including at least Drs. Mariam Jamal-Hanjani and Charles Swanton, conceived, reduced to practice, and communicated these claimed methods to the named inventors of the ’596 Patent.

23. The sole support for the foregoing claimed methods in both Asserted Patents comes from Example 13 in the specification.

24. Example 13, however, describes the TRACERx experiments conceived of by researchers at UCL, including at least Drs. Mariam Jamal-Hanjani and Charles Swanton. The work that appears in Example 13 is also described in Dr. Jamal-Hanjani’s doctoral dissertation regarding the TRACERx study. This is clear from, for example, the figures and lists of genes referred to in Example 13 and claimed by the Asserted Patents, which are identical to those set forth in the doctoral dissertation of Mariam Jamal-Hanjani. *Compare* Jamal-Hanjani Thesis at 155-58 (Tables 22 and 23 and Figure 49) *with* ’454 Patent at Sheets 70, 73-75 (Figures 51A, 53A, 53B, and 54B) and ’596 Patent at Sheets 70, 73-75 (Figures 51A, 53A, 53B, and 54B).

25. On information and belief, Drs. Jamal-Hanjani and Swanton conceived of the research plan for the TRACERx study and provided that plan to Natera during their collaboration. On information and belief, Natera's laboratory systems were used to process samples and detect SNV mutations at the direction of Drs. Jamal-Hanjani and Swanton.

26. Accordingly, the Asserted Patents are invalid for omitting researchers at UCL, including at least Drs. Mariam Jamal-Hanjani and Charles Swanton, as inventors.

TENTH DEFENSE – PROSECUTION LACHES

27. The '454 Patent is unenforceable against NeoGenomics under the doctrine of prosecution laches. The '454 Patent was issued after an unreasonable and unexplained delay in prosecution, and that delay in prosecution prejudiced NeoGenomics, including, for example, evidentiary and economic prejudice.

28. The '454 Patent was filed on May 6, 2022, published on September 8, 2022, and issued on December 20, 2022. The application that issued as the '454 Patent is a continuation of U.S. Application No. 17/692,469, filed on March 11, 2022, which is a continuation of application No. 15/898,145, filed on February 15, 2018, now U.S. Patent No. 11,319,595, which is a continuation of application No. 14/692,703, filed on April 21, 2015, now U.S. Patent No. 10,179,937.

29. U.S. Patent No. 10,179,937 claims priority to provisional application No. 61/982,245, filed on April 21, 2014, provisional application No. 61/987,407, filed on May 1, 2014, provisional application No. 61/994,791, filed on May 16, 2014, provisional application No. 62/066,514, filed on October 21, 2014, provisional application No. 62/146,188, filed on April 10, 2015, provisional application No. 62/147,377, filed on April 14, 2015, and provisional application No. 62/148,173, filed on April 15, 2015.

30. Natera unreasonably delayed pursuing the claims of the '454 patent for at least seven years. *See Sonos, Inc. v. Google LLC*, No. C 20-06754 WHA, 2023 WL 6542320, *16-19, n.7 (N.D. Cal. Oct. 6, 2023) (holding patents unenforceable due to prosecution laches and noting the presumption of unreasonable, inexcusable, and prejudicial delay for delays more than six years). Natera did not pursue claims directed to “performing whole exome sequencing or whole genome sequencing,” performing targeted multiplex amplification “to amplify 10 to 500 target loci,” performing targeted multiplex amplification “to obtain amplicons having a length of 50-150 bases,” or sequencing with a depth of read “of at least 50,000 per target locus” until it filed the '454 patent—approximately seven years after the specification of the '454 patent was first filed as U.S. Patent No. 10,179,937.

31. While NeoGenomics contends that the '454 patent does not provide written description support for the claim limitations outlined above, to the extent Natera disagrees, Natera has not identified any reason why it could not have presented the claims earlier. The specification and figures of the '454 patent are the same as those filed for U.S. Patent No. 10,179,937 and child applications claiming priority to same, and Natera pursued numerous claims in the seven years before it pursued the claims of the '454 patent, including those of the '596 Patent approximately three years earlier.

32. The '596 Patent is also unenforceable against NeoGenomics under the doctrine of prosecution laches. The '596 Patent was issued after an unreasonable and unexplained delay in prosecution, and that delay in prosecution prejudiced NeoGenomics, including, for example, evidentiary and economic prejudice.

33. The '596 Patent was filed on February 28, 2019, published on June 27, 2019, and issued on May 3, 2022. The application that issued as the '596 Patent is a continuation of U.S.

Application No. 16/014,961, filed on June 21, 2018, which is a continuation of U.S. Patent No. 10,179,937.

34. Natera unreasonably delayed pursuing the claims of the '596 patent for at least four years. Natera did not pursue claims the claims of the '596 patent until February 28, 2019—approximately four years after the specification of the '596 patent was first filed as U.S. Patent No. 10,179,937. Moreover, Natera unreasonably delayed until June 1, 2021 to amend the '596 patent to claim “targeted multiplex PCR amplification . . . from the isolated cell-free DNA.”

35. While NeoGenomics contends that the '596 patent does not provide written description support for the claim limitation “targeted multiplex PCR amplification . . . from isolated cell-free DNA,” or any other claim limitation in the '596 patent, to the extent Natera disagrees Natera has not identified any reason why it could not have presented the claims earlier. The specification and figures of the '596 patent are the same as those filed for U.S. Patent No. 10,179,937 and child applications claiming priority to same, and Natera pursued numerous claims before it pursued the claims of the '596 patent.

36. As a result of Natera’s unexplained and unreasonable delay, NeoGenomics has been prejudiced. For example, during the period of delay, NeoGenomics invested \$390 million to acquire Inivata and has invested millions more in additional research and development for the RaDaR assay. Natera’s years of delay in ultimately pursuing claims that it now contends to cover the RaDaR assay is highly prejudicial to NeoGenomics.

37. In addition, as a result of Natera’s unexplained and unreasonable delay in pursuing the claims of the Asserted Patents, the public has suffered prejudice, for example, because other third parties such as ArcherDX Inc. have also made significant investments in the technology described in the asserted patents over the course of several years. Permitting Natera to enforce its

patents after unreasonably delaying prosecution will stifle innovation in the field and take away patient choice in cancer testing and diagnostics.

ELEVENTH DEFENSE – JUDICIAL ESTOPPEL

38. The relief sought by Natera is barred, in whole or in part, by the doctrine of judicial estoppel. As an example, Natera is precluded under the doctrine of judicial estoppel from taking the position relating to “performing targeted multiplex amplification . . . to obtain amplicons” and “sequencing the amplicons” to the extent that those positions are inconsistent with the positions successfully advanced by Natera in IPR2024-00346.

NEOGENOMICS’ COUNTERCLAIMS AGAINST NATERA

In support of its Counterclaims against Natera, NeoGenomics alleges as follows:

NATURE OF THE ACTION

1. In response to Natera’s allegations in the Amended Complaint, NeoGenomics seeks a declaratory judgment that it has not infringed the Asserted Patents, that the Asserted Patents are invalid, and that the Asserted Patents are unenforceable under the Patent Laws of the United States, 35 U.S.C. § 271 *et seq.*

THE PARTIES

2. Natera is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business at 201 Industrial Road, Suite 410, San Carlos, California 94070.

3. NeoGenomics is a corporation organized and existing under the laws of the State of Florida, with its principal place of business at 9490 NeoGenomics Way, Fort Myers, FL 33912.

JURISDICTION AND VENUE

4. The Court has subject matter jurisdiction over NeoGenomics’ declaratory judgment counterclaims pursuant to 28 U.S.C. §§ 2201 and 2202.

5. The Court has personal jurisdiction over Natera because Natera consented to jurisdiction in this District by filing its Amended Complaint in this action.

6. To the extent that venue is proper in the underlying patent infringement action, venue is also proper with respect to NeoGenomics' Counterclaims pursuant to 28 U.S.C. §§ 1391 and 1400(b) and because Natera consented to this venue by filing its Amended Complaint in this action.

FIRST COUNT

(Declaration of Non-Infringement of U.S. Patent 11,530,454)

7. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-6 of its Counterclaims as though fully set therein.

8. Natera has brought an action asserting the '454 Patent against NeoGenomics and has alleged that it is the legal owner of the '454 Patent.

9. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '454 Patent.

10. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '454 Patent.

11. NeoGenomics hereby seeks a declaration that NeoGenomics has not infringed and is not infringing any valid and enforceable claim of the '454 Patent.

12. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

SECOND COUNT

(Declaration of Non-Infringement of U.S. Patent 11,319,596)

13. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-12 of its Counterclaims as though fully set therein.

14. Natera has brought an action asserting the '596 Patent against NeoGenomics and has alleged that it is the legal owner of the '596 Patent.

15. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '596 Patent.

16. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '596 Patent.

17. NeoGenomics hereby seeks a declaration that NeoGenomics has not infringed and is not infringing any valid and enforceable claim of the '596 Patent.

18. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

THIRD COUNT

(Declaration of Invalidity of U.S. Patent 11,530,454)

19. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-18 of its Counterclaims as though fully set therein.

20. Natera has brought an action asserting the '454 Patent against NeoGenomics and has alleged that it is the legal owner of the '454 Patent.

21. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '454 Patent.

22. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '454 Patent.

23. The claims of the '454 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations, and laws pertaining thereof.

24. NeoGenomics incorporates by reference and restates NeoGenomics' Second Affirmative Defense of Invalidity as though fully set forth herein.

25. NeoGenomics hereby seeks a declaration that the claims of the '454 Patent are invalid.

26. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

FOURTH COUNT

(Declaration of Invalidity of U.S. Patent 11,319,596)

27. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-26 of its Counterclaims as though fully set therein.

28. Natera has brought an action asserting the '596 Patent against NeoGenomics and has alleged that it is the legal owner of the '596 Patent.

29. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '596 Patent.

30. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '596 Patent.

31. The claims of the '596 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations, and laws pertaining thereof.

32. NeoGenomics incorporates by reference and restates NeoGenomics' Second Affirmative Defense of Invalidity as though fully set forth herein.

33. NeoGenomics hereby seeks a declaration that the claims of the '596 Patent are invalid.

34. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

FIFTH COUNT

(Declaration of Unenforceability of U.S. Patent 11,530,454)

35. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-34 of its Counterclaims as though fully set therein.

36. Natera has brought an action asserting the '454 Patent against NeoGenomics and has alleged that it is the legal owner of the '454 Patent.

37. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '454 Patent.

38. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '454 Patent.

39. NeoGenomics incorporates by reference and restates NeoGenomics' Ninth Affirmative Defense of Prosecution laches as though fully set forth herein.

40. NeoGenomics hereby seeks a declaration that the claims of the '454 Patent are unenforceable due to prosecution laches.

41. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

SIXTH COUNT

(Declaration of Unenforceability of U.S. Patent 11,319,596)

42. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-41 of its Counterclaims as though fully set therein.

43. Natera has brought an action asserting the '596 Patent against NeoGenomics and has alleged that it is the legal owner of the '596 Patent.

44. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '596 Patent.

45. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '596 Patent.

46. NeoGenomics incorporates by reference and restates NeoGenomics' Ninth Affirmative Defense of Prosecution Laches as though fully set forth herein.

47. NeoGenomics hereby seeks a declaration that the claims of the '596 Patent are unenforceable due to prosecution laches.

48. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

RESERVATION OF RIGHTS

49. NeoGenomics expressly reserves the right to assert any additional defenses or counterclaims that may now exist or in the future may be available based on discovery and further factual investigation in this case.

DEMAND FOR JURY TRIAL

50. NeoGenomics hereby demands a trial by jury of all issues so triable in this action.

REQUEST FOR RELIEF

WHEREFORE, having fully answered the Amended Complaint and having asserted Affirmative Defenses, and Counterclaims, NeoGenomics respectfully requests the following relief:

A. That this Court enter judgment on Natera's Amended Complaint and NeoGenomics's Counterclaims in favor of NeoGenomics, against Natera, with Natera being awarded no relief of any kind in this action;

B. That this Court enter judgment and/or declarations that NeoGenomics does not infringe the Asserted Patents, that the Asserted Patents are invalid, and that the Asserted Patents are unenforceable;

C. That this Court enter a judgment declaring this case exceptional under 35 U.S.C. § 285 and awarding NeoGenomics its attorneys' fees and prejudgment and post-judgment interest;

- D. That this Court award NeoGenomics all of its costs of this action; and
- E. That this Court grant such other and further relief as the Court shall deem just and proper.

This the 20th day of December, 2024

/s/ Matthew I. Kreeger

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83.1(d)